1992), larger versions of the same polypeptide (GVGVP) (SEQ. ID. NO. 2) containing 121 repeats (605 amino acids) or 251 repeats (1255 amino acids) were hyperexpressed in *E. coli* (Guda et al., 1995; Brixey et al., 1997). Bacterial cells showed polymer inclusion bodies occupying up to 90% of their cell volume under optimal conditions (See Figure 1). Production of polymers by fermentation, however, is not cost effective when compared with petroleum based polymers. Therefore, we have recently expressed the GVGVP (SEQ. ID. NO. 2) 120mer in tobacco. Even though lower levels of expression were observed in cultured tobacco cells (Zhang et al., 1995) and some transgenic plants in the F0 generation (probably due to the position effect and heterozygous nature, Zhang et al., 1996), higher levels of polymer expression were observed in transgenic plants after self-crossing in the F1 generation; inclusion bodies have been observed in tobacco cells (see Figure 2), which is a good indication of a very high level of PBP expression (Daniell, 1995; Daniell and Guda, 1997). The transgenic tobacco plants expressing this PBP grew, flowered and produced seeds normally (Zhang et al., 1996). Physiological and ultrastructural studies reveal that transgenic tobacco plants expressing PBP are similar to control untransformed plants.

Please replace paragraph [0014] with the following:

[0014] In contrast we attempt here to express a protein polymer and not a polyester. PBPs used in our study are expressed from a single synthetic gene that can easily be altered to increase the fiber strength, water absorption, thermal properties, elasticity and dye binding capacity of cotton fiber by changing the amino acid composition. We

attempt to accomplish this using a gene encoding $GVGVP_{121}$(SEQ. ID. NO. ~~23~~); this gene has been expressed at high levels in bacteria (Figure 1; Daniell et al., 1997) and tobacco plants (Figure 2; Daniell and Guda, 1997). Transgenic tobacco plants expressing this PBP grew, flowered and produced seeds normally (Zhang et al., 1996). However, this gene has not previously been expressed in cotton fibers.

Marked-Up Version Showing Changes Made to the Claims

1. (Twice Amended) A transgenic cotton plant comprising fiber cells stably transformed with an expression cassette comprising a gene encoding an ~~elastic and plastic protein based polymer wherein said fiber cells exhibit increased water absorption, fiber strength, elasticity, and dye binding capacity relative to untransformed fiber cells~~ amino acid sequence including at least one pentapeptide which is repeated at least once, and which gene does not occur in nature.

3. (Twice Amended) An expression cassette comprising ~~a fiber specific promoter driving expression of a gene encoding an elastic and plastic protein based polymer,~~ a terminator, one or more selectable marker genes , ~~and~~ one or more regulatory elements and a fiber specific promoter which promotes the expression of a coding sequence encoding an amino acid sequence including at least one pentapeptide which is repeated at least once and which coding sequence does not occur in nature, in order to facilitate transformation of plant cells.

4. (Twice Amended) The expression cassette of Claim 3 wherein the ~~elastic and plastic protein based polymer comprises a repetitive amino acid sequence~~pentapeptide which is repeated is Gly-Val-Gly-Val-Pro ~~(SEQ. ID. NO. 2)~~(SEQ ID NO:2).

5. (Twice Amended) The expression cassette of claim 3 wherein said fiber specific promoter ~~comprises~~is an E-6 promoter.

Please add the following new claims:

8. (New) The transgenic cotton plant of Claim 1, wherein said pentapeptide is repeated between 20 and 251 times.

9. (New) The transgenic cotton plant of Claim 1, wherein said pentapeptide is Gly-Val-Gly-Val-Pro (SEQ ID NO:2).

10. (New) The transgenic cotton plant of Claim 8, wherein said pentapeptide is Gly-Val-Gly-Val-Pro (SEQ ID NO:2).

Please cancel Claims 2, 6 and 7 without prejudice and without disclaimer of the subject matter contained therein.

REMARKS

Applicant notes with appreciation the Examiner drawing attention to the need to request entry of the substitute specification, drawings, and abstract. Applicant now hereby formally requests entry of the substitute specification, drawings, and abstract. Claim 1 has been amended to incorporate Claim 2, which now stands canceled. Claims 3-5 have been amended and Claims 6 and 7 have been canceled and new Claim number 8 has been added as supported by paragraph [0010] of the Substitute Specification. No new matter has been added.

Response to § 112 Rejections

Claims 1-7 have been rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification. This rejection is respectfully traversed.

Applicant notes with appreciation the Examiner's helpful comments concerning the enabling description requiring a deposit of plasmids. However, Applicant asserts that the amended claims and Substitute Specification provide an enabling description that would teach one in the art how to perform the Applicant's invention, without depositing the plasmids. Consequently, Applicant asserts that the invention does not require teaching a nucleic acid encoding GVGVP or depositing a set of plasmids, as the nucleic acid sequence encoding GVGVP was known, as shown in Daniell, et al. *Hyperexpression of a Synthetic Protein Based Polymer Gene*, Methods in Molecular Biology 63:359-371 (1997). Since the sequence was known, Applicant need not recite it in the specification. However, if it would be helpful, Applicant proposes to copy the

sequence from the above-referenced article into the specification, as all articles disclosed in the specification were incorporated by reference. A copy of the article is included with this Amendment for the Examiner's review.

It is the expression of GVGVP in a cotton plant via an expression cassette that Applicant discloses as his invention, not GVGVP or any specific nucleic acid that may code for GVGVP. In that sense, such a nucleic acid is only an intermediate, not final product. The instant invention does not need to teach a particular nucleic acid encoding GVGVP, in order for one skilled in the art to deduce a set of nucleic acid sequences encoding GVGVP and use such sequences to transform a cotton plant with an expression cassette comprising a gene encoding GVGVP.

The recommendation to submit a plasmid is appreciated, but the plasmids are obtainable by a repeatable method as set forth in the specification and therefore, Applicant believes such a submission is unnecessary. We invite the Examiner's attention to paragraph [0016] and [0019] of the Substitute Specification.

> A nuclear vector for transient expression of the 120mer gene has been constructed. The plasmid pUC-GUS (obtained from Stratagene) was digested with XbaI and SstI to remove the 1.8 kb XbaI-SstI fragment containing the uidA gene, and the remaining 4.3 kb fragment was ligated with the 1.8 kb 120mer polymer fragment (obtained as XbaI-SstI fragment in pUC118) to produce plasmid pUC-XZ-120mer. The 120mer polymer gene in this construct is driven by the CaMV 35S promoter and flanked by the nos terminator. A nuclear vector for stable expression of the 120mer polymer protein also has been constructed. The uidA gene was removed from the plasmid pBI121 as a XbaI-SstI fragment and replaced by the 120mer polymer fragment (obtained as XbaI-SstI fragment in pUC118 plasmid) resulting in the construct pBI121-XZ-120mer (Figure 3). The 120mer polymer gene in this construct is driven by the CaMV 35S promoter and flanked by the nos terminator. This nuclear vector also contains a nptII gene driven by the nos promoter and flanked by the nos

terminator to facilitate selection of transformed cells or tissues on kanamycin .

Identified fiber genes can be grouped into two types – genes which only express in fibers (fiber-specific genes) and those which express in other tissue types besides fibers. Fiber-specific genes, isolated from cDNA libraries, include a lipid transfer protein gene, the "fiber" gene E6 and Rac 13. However, only the promoter for the E6 gene, isolated from a genomic library, has been well characterized (John, 1995a). In order to avoid possible pleiotropic or epistatic effects of introduced genes, it is desirable to use promoters which will express foreign genes primarily in fiber cells. Therefore, in order to express PBP genes in cotton fibers, the 35S CaMV promoter in recombinant constructs (pBI121-XZ-120mer and pBI-EV35S130mer) is replaced by the E-6 promoter (Figure 4); this will direct expression of foreign genes in a tissue specific and developmentally regulated manner in transgenic cotton plants (John and Crow, 1992). The E6 promoter has been used successfully to express PHB polymers in cotton fiber (John and Keller, 1996).

Clearly one skilled in the art would be able to create the plasmids from the aforementioned paragraphs (again, if in possession of the gene which was known when this application was filed). One skilled in the art is enabled to make the plasmid containing an E-6 promoter to replace the 35S CaMV promoter by following the teaching in paragraphs [0016] and [0019] and then combining that knowledge with the art taught in John '95 and John and Crow '92. This knowledge, along with the plasmid maps of figures 3 and 4, clearly teach one skilled in the art how to make the plasmids which house the expression cassette.

In response to the rejections of Claims 1-7 under 35 U.S.C §112 in paragraph number 7 of the Examiner's response, we have amended Claims 1, and 3-5, canceled Claims 2, and 6-7 and added new Claim 8 to avoid claiming an "elastic and plastic" based polymer. Note that this change was made for compliance with section 112, and not

because Applicant believes the polymers would not be considered elastic or plastic by one skilled in the art. Further, at the helpful suggestion of the Examiner, the claims have been amended to cancel the phrase "increased water absorption, fiber strength, elasticity and dye binding," again for compliance with section 112. Finally the term "repetitive" is canceled to make the pentamer sequence of GVGVP clear. Rather, the claim now claims a fiber cell having a gene encoding a pentameric amino acid sequence which repeats at least once and which gene does not occur in nature as described in *Protein-Based Polymeric Materials (Synthesis and Properties)*, Polymeric Materials Encyclopedia 9:7263-7279, CRC Press (1996) copy enclosed. Support for the non-naturally occurring gene can be found in claim 6 as filed.

Applicant traverses the Examiner's assertion that the claims need to reflect the limitations setting out the use of cultivars. It is well known in the art that one transformable cultivar is used to introduce the gene of interest and the trait is subsequently outcrossed into other useful cultivars. This practice is very common and is used to introduce the trait into virtually any commercial, compatible cultivar.

In response to the rejections of Claims 1-7 under 35 U.S.C §112 in paragraph 8 of the Examiner's response, we have amended Claim 1 to Claim 2 to no longer claim a broad genus of elastic and plastic polymers, and as a result, the Applicant believes the rejection is thereby obviated.

In response to the rejections of Claims 1-7 under 35 U.S.C §112 in paragraph 9 of the Examiner's response Applicant has amended Claims 1 and 3-5 and canceled Claims 6-7 to delete the term "elastic and plastic." Furthermore Applicant has deleted the term

"dye binding capacity," and in Claim 4 Applicant has deleted the term "repetitive." In reference to the rejection of claim 3, Applicant has amended the claim to clarify that the promoter promotes the expression of a coding sequence. The coding sequence and promoter form the gene. Thus Claim 3 should now be considered definite. Finally Claim 6 has been canceled to delete the terms "manipulation" and "synthetic." As a result of the aforementioned changes and responses the Applicant believes the rejections under § 112 are thereby obviated.

102 Rejections

Claims 1, 3 and 5-7 have been rejected under 35 U.S.C. §102(b) as being anticipated by each of John (1997, U.S. Patent 5,602,321) and John et al (1996, Proc. Natl. Acad. Sci. USA 93: 12768-12773. Further, Claims 1, 3 and 5-7 have been rejected under 35 U.S.C. §102(b) as being anticipated by John et al. (1997, US Patent 5,597,718) in light of John et al. (1995, Plant Physiol. 108:669-676). The claims of the present application claim a cotton plant with fiber cells transformed with a gene which does not occur in nature. The John references fail to show such a synthetic gene, or any motivation for fiber cells expressing synthetic genes. Accordingly, Applicant believes these rejections cannot be maintained and respectfully request they be withdrawn.

103 Rejections

Claims 1-7 have been rejected under 35 U.S.C§ 103(a) as being unpatentable over John et al (1997, US Patent 5,597,718) in view of Zhang et al (1996, Plant Cell Rep. 16: 174-179). Applicant respectfully submits that the claims as amended, are clearly patentable over John et al in view of Zhang et al. We respectfully submit that there is no motivation found in the prior art whereby a person of ordinary skill in the field of this invention would insert the sequences of Zhang into fiber cells. John fails to cure this defect. *Gambro Lundia AB v. Baxter Healthcare Corp.*, 42 U.S.P.Q.2d, 1378 (Fed. Cir. 1997), held that the record must show a teaching, suggestion or reason to substitute the claimed invention for the referenced prior art. However, even if shown, it does not obviate the claimed invention which pertains to transformed fiber cells.

Applicant submits that the record does not offer a suggestion, teaching or reason to substitute the GVGVP sequence disclosed in Zhang for the protein based polymer H6 taught in John et al in order to stably transform cotton cells. Zhang makes no reference to cotton plants nor to fiber cells, and offers only a generalized assessment when it declares "the present study demonstrated the feasibility of expressing protein based polymers in plant systems." Without a suggestion to combine, no *prima facie* case of obviousness can stand. Furthermore, the H6 sequence of John is a naturally occurring sequence. There is no motivation to specifically engineer a sequence to use to transform fiber cells. We turn the Examiner's attention to *In re Baird*, 29 USPQ2d 1550 (Fed. Cir. 1994), which held that it is not sufficient that the prior art render the claimed invention obvious to try.

Although *In Re Baird* analyzed whether a claimed chemical compound was obvious, it is applicable to the current situation. The court in *In re Baird* discussed:

> The fact that a claimed chemical compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious. A disclosure of millions of compounds does not render obvious a claim to three compounds.

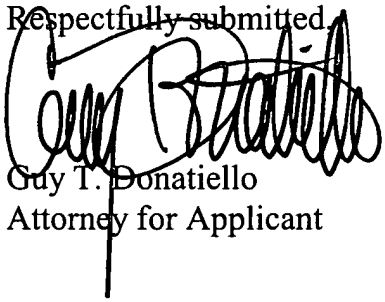
Applicant asserts that because cotton (genus *Gossyium*) and tobacco (genus *Nicotiania*) have different chemical and physical properties, each plant will have a differential response to various stimuli, including the introduction of an amino acid, and finally, tobacco has no fiber cells. Successful expression of GVGVP in tobacco does not equate to GVGVP expression in cotton fiber cells, as tobacco has no such cells and therefore provides no motivation or reason to transform such cells.

Claims 1-7 have been rejected under 35 U.S.C. §103(a) as being unpatentable over John et al (1996 Proc. Natl. Acad. Sci. USA 93:12768-12773 in view of Zhang et al (1996, Plant Cell Rep. 16: 174-179). As a result of the amendments to Claims 1-7, the invention of the Applicant is now clearly defined to remove the rejection, and Applicant respectfully requests this rejection be withdrawn. Applicant further asserts that John et al teaches away from using the amino acid sequence of Zhang et al in cotton plant fiber cells. John et al teaches a multigene construct encoding bioplastic producing bacterial enzymes that help process the polyester, polyhydroxybutyrate (PHB). As previously stated, this is naturally occurring and thus falls outside the scope of the amended claims.

John et al does not contemplate altering the fiber since the polyester created from John et al, is the end product of a bacterial pathway.

In light of the foregoing amendments, we believe that the entire application is now in condition for allowance, which action is respectfully requested.

Respectfully submitted,



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